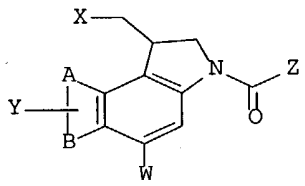
L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:931357 CAPLUS Full-text
DN 140:5036
TI Processes for preparing 3-substituted 1-(chloromethyl)-1,2-dihydro-3h-[ring fused indol-5-yl(amine-derived)] compounds and analogues thereof, and to products obtained therefrom
IN Denny, William Alexander; Yang, Shanjin; Atwell, Graham John; Jeffrey, Scott Charles
PA Auckland Uniservices Limited, N. Z.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097635	A1	20031127	WO 2003-NZ94	20030519

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI NZ 2002-519031 A 20020517
OS MARPAT 140:5036
GI

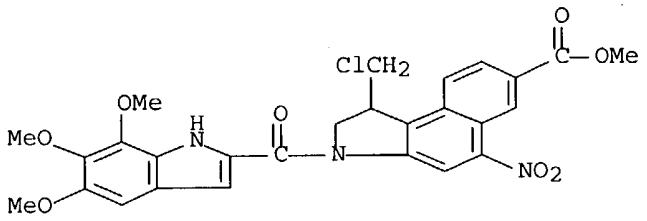


I

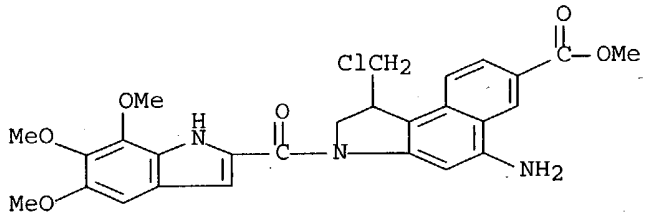
AB The invention provides processes of preparing 3-substituted 1-(chloromethyl)-1,2-dihydro-3H-[ring fused indol-5-yl(amine-derived)] compds. of formula (I) and its analogs, or a physiol. functional derivative thereof, I, wherein A and B together may represent a fused optionally substituted benzene, naphthalene, pyridine, furan or a pyrrole ring, where the optional substituents are represented by Y; X is halogen or OSO2R , and W is selected from NO2, NHOH, N(R3)2NHR3, NHCO2R3, N(phthaloyl) or NH2, or W is further selected from the group -NPJ, wherein J is selected from OH or R, and P is a group which is a substrate suitable for a nitroreductase or carboxypeptidase enzyme. The invention is also directed to the use of compds. of formula I as cytotoxins for cancer therapy and as prodrugs for gene-directed enzyme-prodrug therapy (GDEPT) and antibody-directed enzyme-prodrug therapy (ADEPT).

IT **627105-20-8P 627105-29-7P 627105-31-1P 627105-33-3P 627105-35-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of)

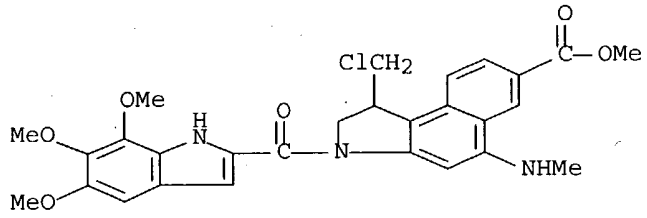
RN 627105-20-8 CAPLUS
CN 1H-Benz[e]indole-7-carboxylic acid, 1-(chloromethyl)-2,3-dihydro-5-nitro-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



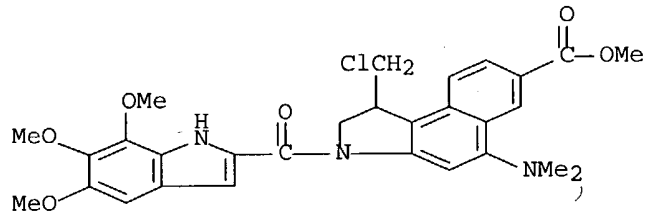
RN 627105-29-7 CAPLUS
CN 1H-Benz[e]indole-7-carboxylic acid, 5-amino-1-(chloromethyl)-2,3-dihydro-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



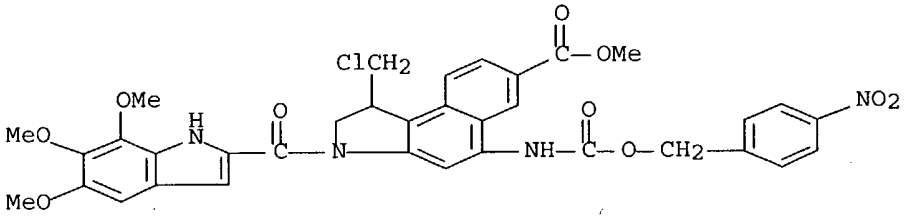
RN 627105-31-1 CAPLUS
CN 1H-Benz[e]indole-7-carboxylic acid, 1-(chloromethyl)-2,3-dihydro-5-(methylamino)-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 627105-33-3 CAPLUS
CN 1H-Benz[e]indole-7-carboxylic acid, 1-(chloromethyl)-5-(dimethylamino)-2,3-dihydro-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI)(CA INDEX NAME)



RN 627105-35-5 CAPLUS
CN 1H-Benz[e]indole-7-carboxylic acid, 1-(chloromethyl)-2,3-dihydro-5-[[[(4-nitrophenyl)methoxy]carbonyl]amino]-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

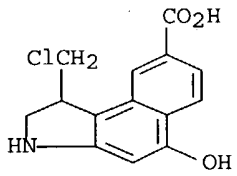
L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:696700 CAPLUS Full-text
DN 139:219341
TI DNA-binding amide-drug conjugates
IN Szekely, Zoltan; Hariprakasha, Humcha Krishnamurthy; Cholody, Marek W.; Michejda, Christopher J.
PA The Government of the United States of America, Represented by the Secretary Department of Health and Human Services, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003072058	A2	20030904	WO 2003-US6006	20030227
WO 2003072058	A3	20040805		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-361050P	P	20020227	
US 2002-370168P	P	20020405	

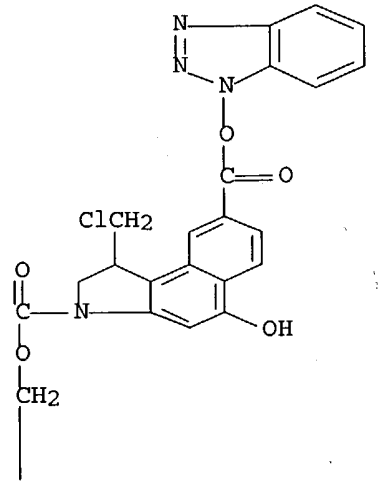
OS MARPAT 139:219341
AB An amide conjugate comprising a DNA intercalator binds to the minor groove of DNA. A composition comprising the conjugate and a carrier is useful for treating cancer in a mammal. Thus, 1-(chloromethyl)-5-hydroxy-1,2-dihydro- 3H-benz[e]indole-8-carboxylic acid (CBIr), a rigid DNA alkylator, was prepared and conjugated to an imidazole-containing derivative
IT **591248-06-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT(Reactant or reagent)(DNA alkylator; DNA-binding polyamide drug conjugates)
RN 591248-06-5 CAPLUS
CN 1H-Benz[e]indole-8-carboxylic acid, 1-(chloromethyl)-2,3-dihydro-5-hydroxy-(9CI) (CA INDEX NAME)



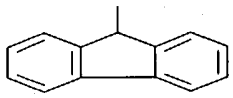
IT **591248-27-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(DNA-binding polyamide drug conjugates)
RN 591248-27-0 CAPLUS
CN 3H-Benz[e]indole-3-carboxylic acid, 8-[(1H-benzotriazol-1-yloxy)carbonyl]-1-(chloromethyl)-1,2-dihydro-5-hydroxy-, 9H-fluoren-9-

ylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



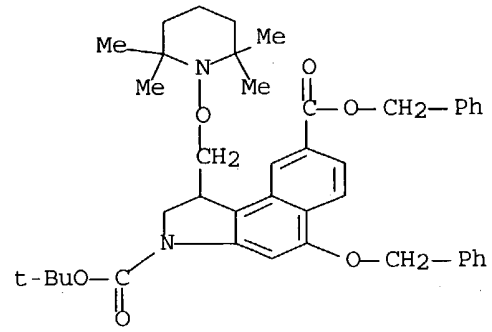
PAGE 2-A



IT **591247-86-8P 591247-87-9P 591247-88-0P**
591247-89-1P 591247-90-4P 591247-91-5P
591247-92-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (in dihydrobenzindolecarboxylic acids preparation; DNA-binding polyamide drug conjugates)

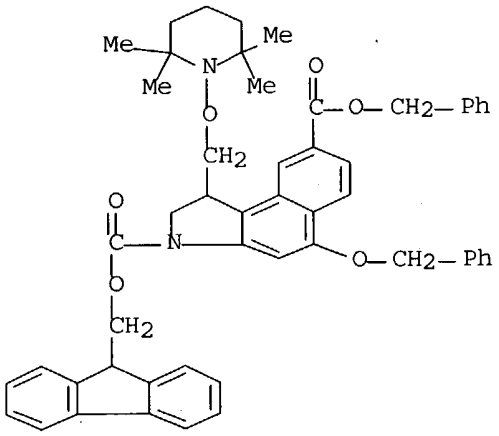
RN 591247-86-8 CAPLUS

CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1,2-dihydro-5-(phenylmethoxy)-1-[[(2,2,6,6-tetramethyl-1-piperidinyl)oxy]methyl]-, 3-(1,1-dimethylethyl) 8-(phenylmethyl) ester (9CI) (CA INDEX NAME)

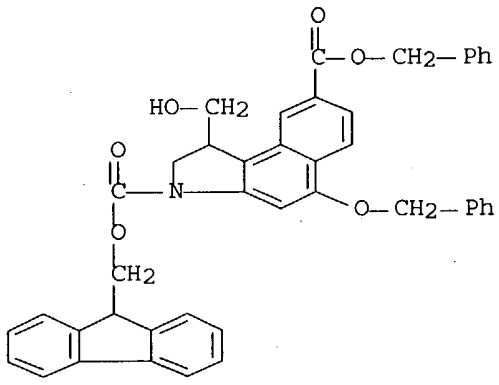


RN 591247-87-9 CAPLUS

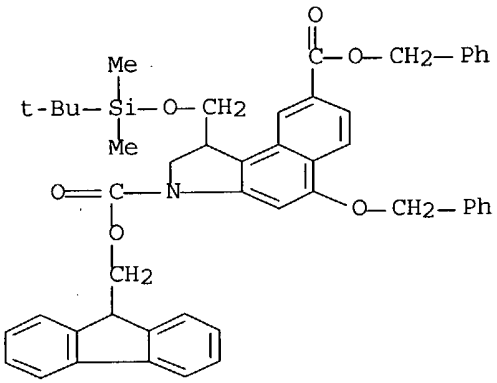
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1,2-dihydro-5-(phenylmethoxy)-1-[[(2,2,6,6-tetramethyl-1-piperidinyl)oxy]methyl]-, 3-(9H-fluoren-9-ylmethyl) 8-(phenylmethyl) ester (9CI) (CA INDEX NAME)



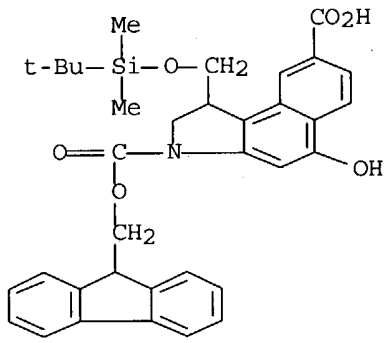
RN 591247-88-0 CAPLUS
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1,2-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 3-(9H-fluoren-9-ylmethyl) 8-(phenylmethyl) ester (9CI) (CA INDEX NAME)



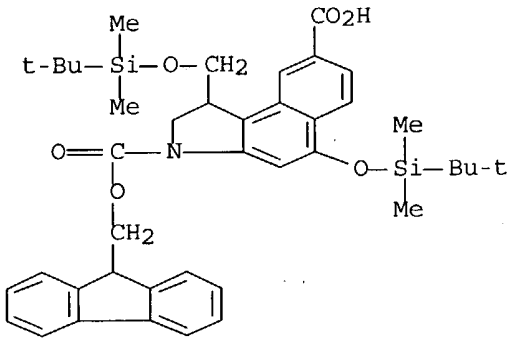
RN 591247-89-1 CAPLUS
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2-dihydro-5-(phenylmethoxy)-, 3-(9H-fluoren-9-ylmethyl) 8-(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 591247-90-4 CAPLUS
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2-dihydro-5-hydroxy-, 3-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

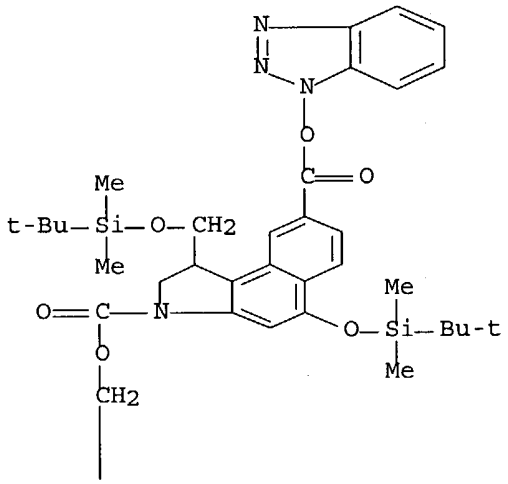


RN 591247-91-5 CAPLUS
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2-dihydro-, 3-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)



RN 591247-92-6 CAPLUS
CN 3H-Benz[e]indole-3-carboxylic acid, 8-[(1H-benzotriazol-1-yloxy)carbonyl]-
5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2-dihydro-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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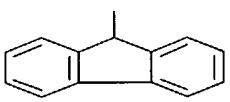
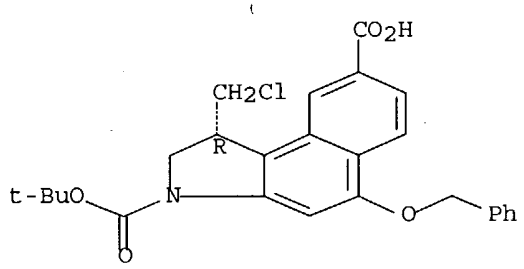


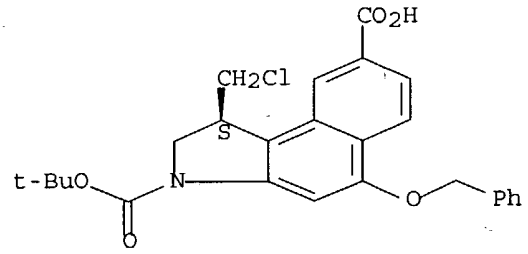
L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:627681 CAPLUS Full-text
DN 135:338739
TI Metal cation complexation and activation of reversed CPyI analogues of CC-1065 and duocarmycin SA: partitioning the effects of binding and catalysis
AU Ellis, David A.; Wolkenberg, Scott E.; Boger, Dale L.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (2001), 123(38), 9299-9306
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The synthesis and examination of a novel class of reversed CPyI analogs of CC-1065 and the duocarmycins are described. Capable of a unique metal cation activation of DNA alkylation, these agents allowed the effects of the DNA binding domain (104-fold increase in DNA alkylation rate and efficiency) to be partitioned into two components: that derived from enhanced DNA binding affinity and selectivity (10-80-fold) and that derived from a contribution to catalysis (250-5000-fold). In addition, the reversed enantiomeric selectivity of these sequence selective DNA alkylating agents provides further strong support for a previously disclosed model where it is the noncovalent binding selectivity of the compds., and not the alkylation subunit or the source of catalysis, that controls the DNA alkylation selectivity.
IT **371248-89-4**
RL: PRP (Properties)
(metal cation complexation and activation of reversed CPyI analogs of CC-1065 and duocarmycin SA)
RN 371248-89-4 CAPLUS
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) ester, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **371248-78-1P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(metal cation complexation and activation of reversed CPyI analogs of CC-1065 and duocarmycin SA)
RN 371248-78-1 CAPLUS
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

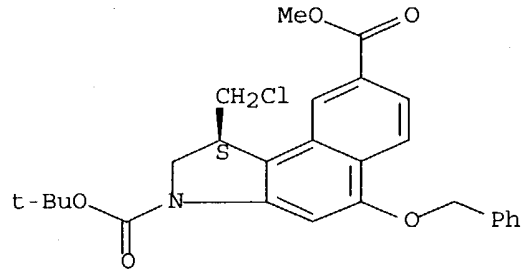


IT **371248-77-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(metal cation complexation and activation of reversed CPyI analogs of CC-1065 and duocarmycin SA)

RN 371248-77-0 CAPLUS

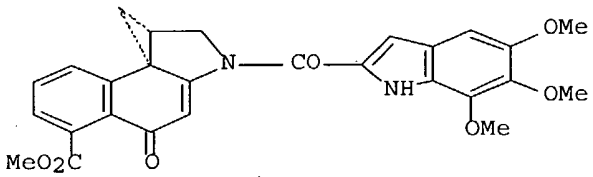
CN 3H-Benz[e]indole-3,8-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) 8-methyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:172344 CAPLUS Full-text
DN 134:340376
TI Synthesis, Chemical Properties, and Biological Evaluation of CC-1065 and Duocarmycin Analogues Incorporating the 5-Methoxycarbonyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one Alkylation Subunit
AU Boger, Dale L.; Hughes, Terry V.; Hedrick, Michael P.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of Organic Chemistry (2001), 66(7), 2207-2216
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 134:340376
GI



I

AB The synthesis of 5-methoxycarbonyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e] indol-4-one (C5-CO2Me-CBI), a substituted CBI derivative bearing a C5 methoxycarbonyl group, and its corresponding 5-hydroxymethyl derivative are described in efforts to establish substituent electronic effects on the agents' functional reactivity and the resulting effect this has on their rate of DNA alkylation. Resolution of an immediate C5-CO2Me-CBI precursor and its incorporation into both enantiomers of analogs of the duocarmycins are also detailed. A study of the solvolysis reactivity and regioselectivity of N-BOC-C5-CO2Me-CBI (12) revealed that the introduction of a C5 Me ester modestly slowed the rate of solvolysis (1.8+, pH 3) without altering the inherent reaction regioselectivity (>20:1). The comparison of the X-ray structures of the N-CO2Me derivs. of C5-CO2Me-CBI and CBI revealed correlations with the reaction regioselectivity and the relative reactivity of the compds. The latter correlated well with the less reactive C5-CO2Me-CBI exhibiting a shortened N2-C2a bond length (1.386 vs 1.390 Å) and smaller χ1 dihedral angle (8.1° vs 21.2°) indicative of greater vinylogous amide conjugation and was accompanied by a diminished (cross-conjugated) cyclopropane conjugation (shorter bond lengths). Establishment of the DNA alkyation properties revealed that C5-CO2Me-CBI-based agents retained the identical alkylation selectivity of the natural products. More importantly, the C5 Me ester was found to decrease the rate (0.77+) of DNA alkylation relative to CBI, consistent with its inherent lower reactivity. These results indicate that the previously observed increase in the rate of DNA alkylation for C7-substituted CBI analogs including CCBI (7-cyano-CBI) is contrary to expectations based on their inherent reactivities. Unlike (I), in which the C5 Me ester does not bind in the minor groove, the C7 substituent lies in the minor groove extending the rigid length of the agents, further enhancing the DNA binding-induced conformational change responsible for activation toward nucleophilic attack and catalysis of the DNA alkylation reaction.

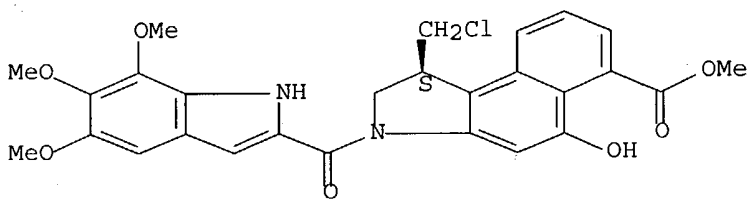
IT **337465-84-6P 337465-94-8P**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, chemical properties, and biol. evaluation of CC-1065 and duocarmycin analogs incorporating the 5-methoxycarbonyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one alkylation subunit)

RN 337465-84-6 CAPLUS

CN 1H-Benz[e]indole-6-carboxylic acid, 1-(chloromethyl)-2,3-dihydro-5-hydroxy-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1S)- (9CI)(CA INDEX NAME)

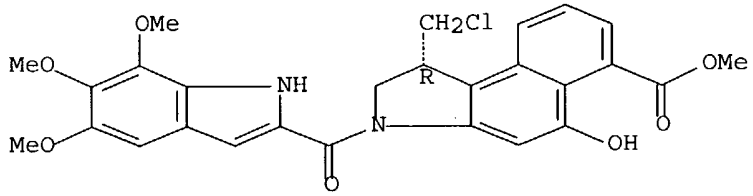
Absolute stereochemistry. Rotation (-).



RN 337465-94-8 CAPLUS

CN 1H-Benz[e]indole-6-carboxylic acid, 1-(chloromethyl)-2,3-dihydro-5-hydroxy-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R)- (9CI)(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



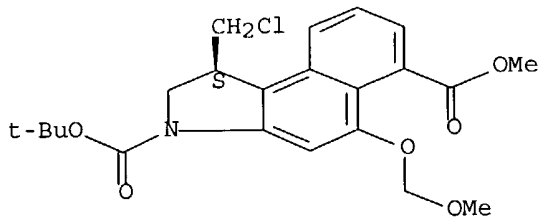
IT **337465-81-3P 337465-91-5P**

RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(synthesis, chemical properties, and biol. evaluation of CC-1065 and duocarmycin analogs incorporating the 5-methoxycarbonyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one alkylation subunit)

RN 337465-81-3 CAPLUS

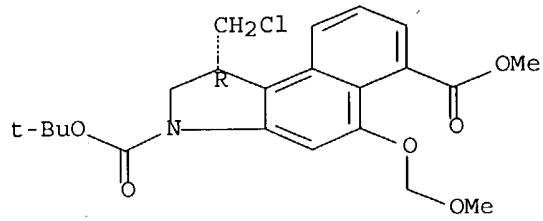
CN 3H-Benz[e]indole-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(methoxymethoxy)-, 3-(1,1-dimethylethyl) 6-methyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



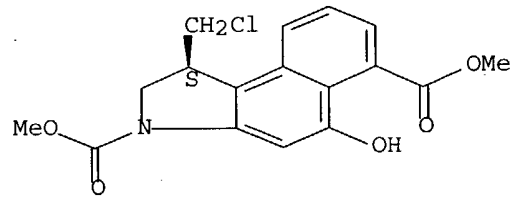
RN 337465-91-5 CAPLUS
CN 3H-Benz[e]indole-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(methoxymethoxy)-, 3-(1,1-dimethylethyl) 6-methyl ester, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



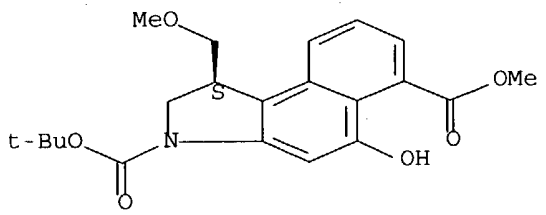
IT **337465-87-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(synthesis, chemical properties, and biol. evaluation of CC-1065 and duocarmycin analogs incorporating the 5-methoxycarbonyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one alkylation subunit)
RN 337465-87-9 CAPLUS
CN 3H-Benz[e]indole-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-hydroxy-, dimethyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



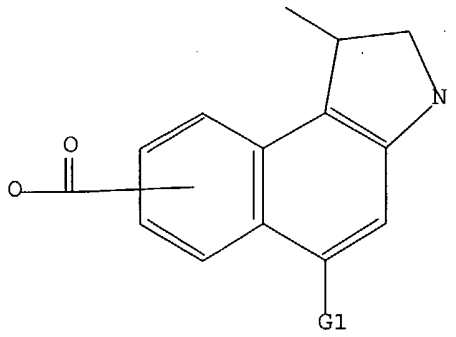
IT **337465-86-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis, chemical properties, and biol. evaluation of CC-1065 and duocarmycin analogs incorporating the 5-methoxycarbonyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one alkylation subunit)
RN 337465-86-8 CAPLUS
CN 3H-Benz[e]indole-3,6-dicarboxylic acid, 1,2-dihydro-5-hydroxy-1-(methoxymethyl)-, 3-(1,1-dimethylethyl) 6-methyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l1; d his; log y
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 16:40:30 ON 09 NOV 2004)

FILE 'REGISTRY' ENTERED AT 16:40:50 ON 09 NOV 2004
L1 STRUCTURE UPLOADED
L2 2 S L1
L3 23 S L1 FUL

FILE 'CAPLUS' ENTERED AT 16:41:21 ON 09 NOV 2004
L4 4 S L3

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	19.48	175.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.80	-2.80

STN INTERNATIONAL LOGOFF AT 16:41:55 ON 09 NOV 2004